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| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) Sheet 1 of 2 | | Complete if Known | |
| | | Application Number | 10/573,131 |
| | | Filing Date | April 18, 2006 |
| | | First Named Inventor | Darrel W. Stafford |
| | | Group Art Unit | 1634 |
| | | Examiner Name | Sitton |
| | | Attorney Docket No. | 5470-401 |



| U.S. PATENTS AND PATENT PUBLICATIONS | | | | | |
|--------------------------------------|----------|----------------------|-------------------------|---|---|
| Examiner Initials* | Cite No. | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
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| U.S. PATENT APPLICATIONS | | | | |
|--------------------------|----------|-----------------|-------------------------------------|--|
| Examiner Initials* | Cite No. | U.S. Serial No. | Name of Applicant of Cited Document | Date of Filing of Cited Document MM-DD-YYYY |
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| FOREIGN PATENT DOCUMENTS | | | | | | | |
|--------------------------|----------|-------------------------|--------|-------------------------|---|---|-------------|
| Examiner Initials* | Cite No. | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Translation |
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| OTHER NON PATENT LITERATURE DOCUMENTS | | | | | |
|---------------------------------------|----------|--|--|--|---|
| Examiner Initials* | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T |
| | 1. | Absher et al. "Patient-Specific Factors Predictive of Warfarin Dosage Requirements" <i>Ann Pharmacother</i> 36(10):1512-1517 (2002) | | | |
| | 2. | Chenhsu et al. "Long-Term Treatment with Warfarin in Chinese Population" <i>Ann Pharmacother</i> 34(12):1395-1401 (2000) | | | |
| | 3. | Devlin et al. "A Comparison of Linkage Disequilibrium Measures for Fine-Scale Mapping" <i>Genomics</i> 29(2):311-322 (1995) | | | |
| | 4. | Durrin et al. "Vitamin D receptor 3'-untranslated region polymorphisms: lack of effect on mRNA stability" <i>Biochimica et Biophysica Acta</i> 1453(3):311-320 (1999) | | | |
| | 5. | Fang et al. "National Trends in Antiarrhythmic and Antithrombotic Medication Use in Atrial Fibrillation" <i>Arch Intern Med</i> 164(1):55-60 (2004) | | | |
| | 6. | Himly et al. "Defective Vaccinia Virus as a Biologically Safe Tool for the Overproduction of Recombinant Human Secretory Proteins" <i>Protein Expression and Purification</i> 14(3):317-326 (1998) | | | |
| | 7. | Hirsh et al. "Antithrombotic therapy in deep vein thrombosis and pulmonary embolism" <i>American Heart Journal</i> 123(4, Pt. 2):1115-1122 (1992) | | | |
| | 8. | Jones et al. "A Cellular DNA-Binding Protein That Activates Eukaryotic Transcription and DNA Replication" <i>Cell</i> 48(1):79-89 (1987) | | | |
| | 9. | Kirchheiner et al. "Clinical consequences of cytochrome P450 2C9 polymorphisms" <i>Clinical Pharmacology & Therapeutics</i> 77(1):1-16 (2005) | | | |
| | 10. | Landefeld et al. "Anticoagulant-Related Bleeding: Clinical Epidemiology, Prediction, and Prevention" <i>The American Journal of Medicine</i> 95(3):315-328 (1993) | | | |
| | 11. | Loebstein et al. "Interindividual variability in sensitivity to warfarin - Nature or nurture?" <i>Clinical Pharmacology & Therapeutics</i> 70(2):159-164 (2001) | | | |
| | 12. | Mountford et al. "Internal ribosome entry sites and dicistronic RNAs in mammalian transgenesis" <i>Trends Genet.</i> 11(5):179-184 (1995) | | | |
| | 13. | Pechlaner et al. "A New Case of Combined Deficiency of Vitamin K Dependent Coagulation Factors" <i>Thrombosis and Haemostasis</i> 68(5):617 (1992) | | | |
| | 14. | Pennisi, Elizabeth "A Closer Look at SNPs Suggests Difficulties" <i>Science</i> 281(5834):1787-1789 (1998) | | | |
| | 15. | Stanley et al. "Identification of a vitamin K-dependent carboxylase in the venom duct of a <i>Conus</i> snail" <i>FEBS Letters</i> 407(1):85-88 (1997) | | | |
| | 16. | Suttie et al. "Mechanisms of action of vitamin K: synthesis of gamma-carboxyglutamic acid" <i>CRC Crit Rev. Biochem</i> 8(2):191-223 (1980) | | | |

| | | | |
|--------------------|--|-----------------|---------|
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| Examiner Name | Sitton | | |
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| 9 | 17. | Wallin et al. "Purification of Warfarin-Sensitive Vitamin K Epoxide Reductase" <i>Methods in Enzymology</i> 282:395-408 (1997) | |
| 9 | 18. | Wu et al. "Characterization of the γ -Glutamyl Carboxylase" <i>Thrombosis and Haemostasis</i> 78(1):599-604 (1997) | |

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|--------------------|----------------------|-----------------|---------|
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|--------------------|----------|----------------------|----------------------|---|---|
| | | Number | Kind Code (if known) | | |
| JP | 1. | 4,736,866 | | Leder et al. | 4/12/1998 |
| | 2. | 4,816,397 | | Boss et al. | 3/28/1989 |
| | 3. | 4,816,567 | | Cabilly et al. | 3/28/1989 |
| | 4. | 5,547,835 | | Koster et al. | 8/20/1996 |
| | 5. | 5,583,278 | | Alt. et al. | 12/10/1996 |
| | 6. | 5,625,122 | | Mak | 4/29/1997 |
| | 7. | 5,698,765 | | Mak | 12/26/1997 |
| | 8. | 5,750,825 | | Yazaki et al. | 5/12/1998 |
| | 9. | 6,043,031 | | Koster et al. | 3/28/2000 |
| | 10. | 6,492,115 | | Guida et al. | 12/10/2002 |
| | 11. | US 2005/0164367 | | Fenge et al. | 7/28/2005 |
| | 12. | US 2006/0166239 | | Chen et al. | 7/27/2006 |
| | 13. | US 2006/0194284 | | Oldenburg et al. | 8/31/2006 |
| | 14. | US 2007/0009950 | | Stafford et al. | 1/11/2007 |

FOREIGN PATENT DOCUMENTS

| Examiner Initials* | Cite No. | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Translation |
|--------------------|----------|-------------------------|----------------|----------------------|---|---|---------------|
| | | Office | Number | Kind Code (if known) | | | |
| JP | 15. | DE | 406 26 040 | | Becker et al. | 1/4/1998 | No |
| | 16. | EP | 0 368 684 | B1 | Medical Research Council | 5/16/1990 | |
| | 17. | EP | 0 127 839 | B1 | Texas A & M University System | 12/12/1984 | |
| | 18. | EP | 0 154 133 | B1 | Genentech, Inc. | 9/11/1985 | |
| | 19. | EP | 0 549 721 | B1 | The Texas A & M University System | 7/07/1993 | |
| | 20. | PCT | WO 88/01649 | | Genex Corporation | 3/10/1988 | |
| | 21. | PCT | WO 93/06213 | | Medical Research Council | 4/01/1993 | |
| | 22. | PCT | WO 95/34679 | | The Gov't of the United States | 12/21/1995 | |
| | 23. | PCT | WO 97/49802 | | Becker et al. | 12/31/1997 | Abstract only |
| | 24. | PCT | WO 98/24884 | | Genpharm International | 6/11/1998 | |
| | 25. | PCT | WO 99/43003 | | Micron Technology, Inc. | 8/26/1999 | |
| | 26. | PCT | WO 00/03015 | | Incyte Pharmaceuticals | 1/20/2000 | |
| | 27. | PCT | WO 2005/030039 | | Stafford et al. | 4/07/2005 | |
| | 28. | PCT | WO 2006/044686 | | Rieder et al. | 4/27/2006 | |
| | 29. | PCT | WO 2006/101474 | | Stafford et al. | 9/28/2006 | |

OTHER NON PATENT DOCUMENTS

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|--------------------|----------|--|---|
| JP | 30. | Altschul et al. "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs" <i>Nucleic Acids Research</i> 25(17):3389-3402 (1997) | |
| | 31. | Bandyopadhyay et al. "γ-Glutamyl carboxylation: An extracellular posttranslational modification that antedates the divergence of mollusks, arthropods, and chordates" <i>PNAS</i> 99(3):1264-1269 (2002) | |
| | 32. | Bell et al. "Warfarin and the inhibition of vitamin K activity by an oxide metabolite" <i>Nature</i> 237:32-33 (1972) | |
| | 33. | Berkner et al. "The Vitamin K-Dependent Carboxylase" <i>J. Nutr.</i> 130:1877-1880 (2000) | |
| | 34. | Blann et al. "Racial background is a determinant of average warfarin dose required to maintain the INR between 2.0 and 3.0" <i>Br J Haematol.</i> 107(1):207-209 (1999) | |

Examiner Signature

Johanne Sitt

Date Considered

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| | |
|-----|---|
| 35. | Boneh et al. "Hereditary Deficiency of Vitamin K-Dependent Coagulation Factors With Skeletal Abnormalities" <i>American Journal of Medical Genetics</i> 65:241-243 (1996) |
| 36. | Brenner et al. "A Missense Mutation in γ -Glutamyl Carboxylase Gene Causes Combined Deficiency of All Vitamin K-Dependent Blood Coagulation Factors" <i>Blood</i> 92(12):4554-4559 (1998) |
| 37. | Cain et al. "Assembly of the Warfarin-sensitive Vitamin K 2,3-Epoxy Reductase Enzyme Complex in the Endoplasmic Reticulum Membrane" <i>The Journal of Biological Chemistry</i> 272(46):29068-29075 (1997) |
| 38. | Cain et al. "Warfarin Resistance Is Associated with a Protein Component of the Vitamin K 2,3-Epoxy Reductase Enzyme Complex in Rat Liver" <i>Thromb Haemost</i> 80:128-33 (1998) |
| 39. | Camire et al. "Enhanced γ -Carboxylation of Recombinant Factor X Using a Chimeric Construct Containing the Prothrombin Propeptide" <i>Biochemistry</i> 39:14322-14329 (2000) |
| 40. | Carter et al. "Prothrombin G20210A is a bifunctional gene polymorphism" <i>Thromb Haemost.</i> 87(5):846-853(2002) |
| 41. | Chu et al. "A Mutation in the Propeptide of Factor IX Leads to Warfarin Sensitivity by a Novel Mechanism" <i>J. Clin. Invest.</i> 98(7):1619-1625 (1996) |
| 42. | Chu et al. "Purified vitamin K epoxide reductase alone is sufficient for conversion of vitamin K epoxide to vitamin K and vitamin K to vitamin K ₂ " <i>PNAS</i> 103(51):19308-19313 (2006) |
| 43. | Copy of International Search Report for PCT/EP2006/000734, dated May 11, 2006 |
| 44. | Crawford et al. "Haplotype Diversity across 100 Candidate Genes for Inflammation, Lipid Metabolism, and Blood Pressure Regulation in Two Populations" <i>Am J. Hum. Genet.</i> 74:610-622 (2004) |
| 45. | Derian et al. "Inhibitors of 2-Ketoglutarate-dependent Dioxygenases Block Aspartyl β -Hydroxylation of Recombinant Human Factor IX in Several Mammalian Expression Systems" <i>The Journal of Biological Chemistry</i> 264(12):6615-6618 (1989) |
| 46. | Dockal et al. "Five recombinant fragments of human serum albumin-tools for the characterization of the warfarin binding site" <i>Protein Sci.</i> 9:1455-1465 (2000) |
| 47. | Dockal et al. "The Three Recombinant Domains of Human Serum Albumin" <i>The Journal of Biological Chemistry</i> 274(41):29303-29310 (1999) |
| 48. | Drysdale et al. "Complex promoter and coding region β 2-adrenergic receptor haplotypes alter receptor expression and predict <i>in vivo</i> responsiveness" <i>PNAS</i> 97(19):10483-10488 (2000) |
| 49. | Esmon et al. "The Functional Significance of Vitamin K Action" <i>The Journal of Biological Chemistry</i> 250(11):4095-4099 (1975) |
| 50. | Esmon et al. "The New Carboxylation Reaction" <i>The Journal of Biological Chemistry</i> 250(12):4744-4748 (1975) |
| 51. | Fasco et al. "Formation of Hydroxyvitamin K by Vitamin K Epoxide Reductase of Warfarin-resistant Rats" <i>The Journal of Biological Chemistry</i> 258(7):4372-4380 (1983) |
| 52. | Fasco et al. "Warfarin Inhibition of Vitamin K 2,3-Epoxy Reductase in Rat Liver Microsomes" <i>Biochemistry</i> 22:5655-5660 (1983) |
| 53. | Furie et al. "The Molecular Basis of Blood Coagulation" <i>Cell</i> 53:505-518 (1988) |
| 54. | Furie et al. "Vitamin K-Dependent Biosynthesis of γ -Carboxyglutamic Acid" <i>Blood</i> 93(6):1798-1808 (1999) |
| 55. | Gage et al. "Adverse Outcomes and Predictors of Underuse of Antithrombic Therapy in Medicare Beneficiaries with Chronic Atrial Fibrillation" <i>Stroke</i> 31:822-827 (2000) |
| 56. | Gage et al. "Use of pharmacogenetics and clinical factors to predict the maintenance dose of warfarin" <i>Thromb Haemost.</i> 91(1):87-94 (2004) |
| 57. | GenBank Accession No. AC135050, <i>Homo sapiens</i> chromosome 16 clone RP11-196G11, complete sequence, October 5, 2002 |
| 58. | GenBank Accession No. AK002742, <i>Mus musculus</i> adult male kidney cDNA, clone:0610033K05, July 10, 2000 |
| 59. | GenBank Accession No. AK013996, <i>Mus musculus</i> 13 days embryo head cDNA, clone:3110005B16, July 10, 2000 |
| 60. | GenBank Accession No. AV003686, <i>Mus musculus</i> C57BL/8J kidney <i>Mus musculus</i> cDNA, clone:0610033K05, Unpublished 1999 |

Examiner Signature

Shane Siff

Date Considered

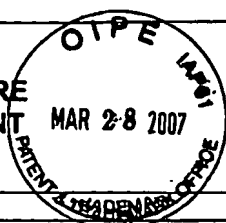
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| | |
|-----|---|
| 61. | GenBank Accession No. AV162712, <i>Mus musculus</i> head C57BL/6 13-dat embryo <i>Mus Musculus</i> cDNA, clone:3110005B16, Unpublished 1999 |
| 62. | GenBank Accession No. AY587020, <i>Homo sapiens</i> vitamin K epoxide reductase complex, March 31, 2004 |
| 63. | GenBank Accession No. BC000828, <i>Homo sapiens</i> vitamin K epoxide reductase complex, CDNA clone IMAGE:3455200, November 15, 2000 |
| 64. | GenBank Accession No. BC002911.1, <i>Homo sapiens</i> , clone MGC:11276, February 5, 2001 |
| 65. | GenBank Accession No. BC002911.2, <i>Homo sapiens</i> vitamin K epoxide reductase complex, clone MGC:11276, February 5, 2001 |
| 66. | GenBank Accession No. BC027734, <i>Homo sapiens</i> vitamin K-epoxide reductase complex, clone MGC:29720, April 8, 2002 |
| 67. | GenBank Accession No. BY703248, adult male kidney <i>Mus musculus</i> , clone 0610033K05, December 16, 2002 |
| 68. | GenBank Accession No. NG_005631, <i>Homo sapiens</i> vitamin K epoxide reductase complex, LOC441241, derived from AC073210.8, <i>Homo sapiens</i> BAC clone RP11-460N20, complete sequence, June 10, 2000 |
| 69. | GenBank Accession No. NM_178600, <i>Mus musculus</i> vitamin K epoxide reductase complex, Vkorc1, derived from AK003237.1, <i>Mus musculus</i> 18-day embryo whole body cDNA, clone:1110001K05, July 10, 2000 and CD774813.1, NIH_BMAP_MHI <i>Mus musculus</i> cDNA clone, July 2, 2003 |
| 70. | GenBank Accession No. NM_178600.2, <i>Mus musculus</i> vitamin K epoxide reductase complex, Vkorc1, March 16, 2004 |
| 71. | GenBank Accession No. NM_024006.1, <i>Homo sapiens</i> hypothetical protein, IMAGE 3455200, October 5, 2003 |
| 72. | GenBank Accession No. NM_024006.4, <i>Homo sapiens</i> vitamin K epoxide reductase complex, VKORC1, March 11, 2007 |
| 73. | GenBank Accession No. NM_203335, <i>Rattus norvegicus</i> vitamin K epoxide reductase complex, Vkorc1, derived from CB314647.1, NICHDR_Rr_Pit1 <i>Rattus norvegicus</i> cDNA clone, IMAGE:6890244, March 3, 2003, AY423047.1, <i>Rattus norvegicus</i> vitamin K epoxide reductase complex subunit 1(Vkorc1) mRNA, complete cds, Sept. 25, 2003 and AW253787.1, UI-R-BJO-acz-d-05-0-UI.s1 UI-R-BJO <i>Rattus norvegicus</i> cDNA clone, December 17, 1999 |
| 74. | GenBank Accession No. NM_206807, <i>Gallus gallus</i> vitamin K epoxide reductase complex, VKORC1, derived from AW355622, <i>Gallus gallus</i> cDNA clone pf1c.pk003.d10, June 23, 2006, and BU114821.1, CHSEQCHL14 <i>Gallus gallus</i> cDNA clone ChEST105p15, November 25, 2002 |
| 75. | GenBank Accession No. NM_206824, <i>Homo sapiens</i> vitamin K epoxide reductase complex, VKORC1, derived from BI822140.1, 603039843F1 NIH_MGC_115 <i>Homo sapiens</i> cDNA clone IMAGE:5180554, October 4, 2001, AK129513.1, <i>Homo sapiens</i> cDNA FLJ26002 fis, clone DMC07743, July 31, 2003 and CD249837.1, NIH_MGC_172 <i>Homo sapiens</i> cDNA, Unpublished 1999 |
| 76. | GenBank Accession No. NP_848715, vitamin K epoxide reductase complex, subunit 1 [<i>Mus musculus</i>], derived from AK003237.1, <i>Mus musculus</i> 18-day embryo whole body cDNA, clone:1110001K05, July 10, 2000 and CD774813.1, NIH_BMAP_MHI <i>Mus musculus</i> cDNA clone, July 2, 2003 |
| 77. | Swiss-Prot Accession No. Q9CRC0, Vitamin K epoxide reductase complex subunit 1 (Vitamin K1 2,3-epoxide reductase subunit 1), Jun 1, 2001 |
| 78. | Goldsmith et al. "Studies on a Family with Combined Functional Deficiencies of Vitamin K-dependent Coagulation Factors" <i>J. Clin. Invest.</i> 69:1253-1260 (1982) |
| 79. | Gossen et al. "Inducible gene expression systems for higher eukaryotic cells" <i>Current Opinion in Biotechnology</i> 5:516-520 (1994) |
| 80. | Greaves et al. "Heritable Resistance to Warfarin in Rats" <i>Nature</i> 215:877-878 (1967) |
| 81. | Guenther et al. "Co-purification of Microsomal Epoxide Hydrolase with the Warfarin-Sensitive Vitamin - K1 Oxide Reductase of the Vitamin K Cycle" <i>Biochemical Pharmacology</i> 55:169-175 (1998) |
| 82. | Hacker et al. "Lack of association between an interleukin-1 receptor antagonist gene polymorphism and ulcerative colitis" <i>Gut</i> 40:623-627 (1997) |
| 83. | Hallgren et al. "Carboxylase overexpression effects full carboxylation but poor release and secretion of factor IX: implications for the release of vitamin K-dependent proteins" <i>Biochemistry</i> 41(50):15045-55 (2002) |


Examiner Signature

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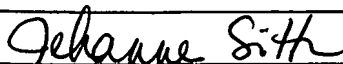
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| | |
|------|---|
| 84. | Higashi et al. "Association between CYP2C9 genetic variants and anticoagulation-related outcomes during warfarin therapy" <i>JAMA</i> 287(13):1690-1698 (2002) |
| 85. | Hirsh et al. "Oral Anticoagulants: Mechanism of Action, Clinical Effectiveness, and Optimal Therapeutic Range" <i>Chest</i> 119:8s-21s (2001) |
| 86. | Houben et al. "Osteocalcin binds tightly to the γ -glutamylcarboxylase at a site distinct from that of the other known vitamin K-dependent proteins" <i>Biochem. J.</i> 341:265-269 (1999) |
| 87. | Huisse et al. "Mechanism of the Abnormal Vitamin K-dependent γ -Carboxylation Process in Human Hepatocellular Carcinomas" <i>Cancer</i> 74:1533-41 (1994) |
| 88. | Jackson et al. "Identification of a consensus motif for retention of transmembrane proteins in the endoplasmic reticulum" <i>The EMBO Journal</i> 9(10):3153-3162 (1990) |
| 89. | Johnson et al. "Characterization of a Variant Prothrombin in a Patient Congenitally Deficient in Factors II, VII, IX, and X" <i>British Journal of Haematology</i> 44:461-469 (1980) |
| 90. | Kaminsky et al. "Correlation of human cytochrome P4502C substrate specificities with primary structure: warfarin as a probe" <i>Mol Pharmacol.</i> 43(2):234-239 (1993) |
| 91. | Kaminsky et al. "Human hepatic cytochrome P-450 composition as probed by <i>in vitro</i> microsomal metabolism of warfarin" <i>Drug Metab Dispos.</i> 12(4):470-477 (1984) |
| 92. | Kaufman et al. "Expression, Purification, and Characterization of Recombinant γ -Carboxylated Factor IX Synthesized in Chinese Hamster Ovary Cells" <i>The Journal of Biological Chemistry</i> 261(21):9622-9628 (1986) |
| 93. | Kohn et al. "Genomic assignment of the warfarin resistance locus, <i>Rw</i> , in the rat" <i>Mammalian Genome</i> 10:696-698 (1999) |
| 94. | Kozak et al. "An analysis of 5'-noncoding sequences from 699 vertebrate messenger RNAs" <i>Nucleic Acids Research</i> 15(20):8125-8148 (1987) |
| 95. | Laupacis et al. "Antithrombotic therapy in atrial fibrillation" <i>Chest</i> 114:579s-589s (1998) |
| 96. | Lee et al. "Glucocorticoids regulate expression of dihydrofolate reductase cDNA in mouse mammary tumour virus chimaeric plasmids" <i>Nature</i> 294:228-232 (1981) |
| 97. | Lesko et al. "Translation of pharmacogenomics and pharmacogenetics: a regulatory perspective" <i>Nat Rev Drug Discov.</i> 3(9):763-769 (2004) |
| 98. | Li et al. "Identification of a <i>Drosophila</i> Vitamin K-dependent γ -Glutamyl Carboxylase" <i>The Journal of Biological Chemistry</i> 275:18291-18296 (2000) |
| 99. | Lin et al. "Binding of the Factor IX γ -Carboxyglutamic Acid Domain to the Vitamin K-dependent γ -Glutamyl Carboxylase Active Site Induces an Allosteric Effect That May Ensure Processive Carboxylation and Regulate the Release of Carboxylated Product" <i>The Journal of Biological Chemistry</i> 279(8):6560-6566 (2004) |
| 100. | Lin et al. "The Putative Vitamin K-dependent γ -Glutamyl Carboxylase Internal Propeptide Appears to Be the Propeptide Binding Site" <i>The Journal of Biological Chemistry</i> 277(32):28584-28591 (2002) |
| 101. | Malhotra et al. "The Kinetics of Activation of Normal and γ -Carboxyglutamic Acid-deficient Prothrombins" <i>The Journal of Biological Chemistry</i> 260(1):279-287 (1985) |
| 102. | Manfioletti et al. "The Protein Encoded by a Growth Arrest-Specific Gene (<i>gas6</i>) Is a New Member of the Vitamin K-Dependent Proteins Related to Protein S, a Negative Coregulator in the Blood Coagulation Cascade" <i>Molecular and Cellular Biology</i> 13(8):4976-4985 (1993) |
| 103. | Mann et al. "Cofactor proteins in the assembly and expression of blood clotting enzyme complexes" <i>Annu Rev Biochem.</i> 57:915-56 (1988) |
| 104. | Martin et al. "Warfarin-resistance genotype determination in the Norway rat, <i>Rattus norvegicus</i> " <i>Laboratory Animals</i> 13:209-214 (1979) |
| 105. | Massari et al. "Helix-Loop-Helix Proteins: Regulators of Transcription in Eucaryotic Organisms" <i>Molecular and Cellular Biology</i> 20(2):429-440 (2000) |
| 106. | McGraw et al. "Evidence for a prevalent dimorphism in the activation peptide of human coagulation factor IX" <i>Proc. Natl. Acad. Sci. USA</i> 82:2847-2851 (1985) |
| 107. | McManus et al. "Gene Silencing in Mammals by Small Interfering RNAs" <i>Nature Reviews</i> 3:737-747 (2002) |
| 108. | McMillan et al. "Congenital Combined Deficiency of Coagulation Factors II, VII, IX, and X" <i>Medical Intelligence</i> 274(23):1313-1315 (1966) |
| 109. | Moor et al. "Coagulation Factor VII Mass and Activity in Young Men With Myocardial Infarction at a Young Age" <i>Arteriosclerosis, Thrombosis, and Vascular Biology</i> 15:655-664 (1995) |

| | | | |
|--------------------|---|-----------------|---------|
| Examiner Signature |  | Date Considered | 5/22/07 |
|--------------------|---|-----------------|---------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Sheet 5 of 7



Complete If Known

| | |
|------------------------|--------------------|
| Application Number | 10/573,131 |
| Filing Date | April 18, 2006 |
| First Named Inventor | Darrel W. Stafford |
| Group Art Unit | 1634 |
| Examiner Name | J. Sitton |
| Attorney Docket Number | 5470-401 |

| | |
|------|---|
| 110. | Morris et al. "Processive Post-translational Modification" <i>The Journal of Biological Chemistry</i> 270(51):30491-30498 (1995) |
| 111. | Morris et al. "Characterization of the Purified Vitamin K-dependent γ -Glutamyl Carboxylase" <i>The Journal of Biological Chemistry</i> 268(12):8735-8742 (1993) |
| 112. | Morrissey et al. "Quantitation of Activated Factor VII Levels in Plasma Using a Tissue Factor Mutant Selectively Deficient in Promoting Factor VII Activation" <i>Blood</i> 81(3):734-744 (1993) |
| 113. | Mumberg et al. "Regulatable promoters of <i>Saccharomyces cerevisiae</i> : comparison of transcriptional activity and their use for heterologous expression" <i>Nucleic Acids Research</i> 22(25):5767-5768 (1994) |
| 114. | Mukharji et al. "Purification of a vitamin K epoxide reductase that catalyzes conversion of vitamin K 2,3-epoxide to 3-hydroxy-2-methyl-3-phytyl-2,3-dihydronaphthoquinone" <i>Proc. Natl. Acad. Sci. USA</i> 82:2713-2717 (1985) |
| 115. | Mutero et al. "Resistance-associated point mutations in insecticide-insensitive acetylcholinesterase" <i>Proc. Natl. Acad. Sci.</i> 91:5922-5926 (1994) |
| 116. | Mutucumarana et al. "A Conserved Region of Human Vitamin K-dependent Carboxylase Residues 393 and 404 is Important for Its Interaction with the Glutamate Substrate" <i>The Journal of Biological Chemistry</i> 278:46488-46493 (2003) |
| 117. | Mutucumarana et al. "Expression and Characterization of the Naturally Occurring Mutation L394R in Human γ -Glutamyl Carboxylase" <i>The Journal of Biological Chemistry</i> 275(42):32572-32577 (2000) |
| 118. | Nellen et al. "What makes an mRNA anti-sense-litve" <i>TIBS</i> 18:419-423 (1993) |
| 119. | Nelsestuen et al. "Role of γ -Carboxyglutamic Acid" <i>The Journal of Biological Chemistry</i> 251(22):6886-6893 (1976) |
| 120. | Nelsestuen et al. "The Mode of Action of Vitamin K" <i>The Journal of Biological Chemistry</i> 249(19):6347-6350 (1974) |
| 121. | Oldenburg et al. "Congenital Deficiency of Vitamin K Dependent Coagulation Factors in Two Families Presents as a Genetic Defect of the Vitamin K-Epoxide-Reductase-Complex" <i>Thromb Haemost</i> 84:937-941 (2000) |
| 122. | O'Reilly et al. "Hereditary Transmission of Exceptional Resistance to Coumarin Anticoagulant Drugs" <i>The New England Journal of Medicine</i> 271:809-815 (1964) |
| 123. | O'Reilly et al. "The Second Reported Kindred With Hereditary Resistance to Oral Anticoagulant Drugs" <i>The New England Journal of Medicine</i> 282:1448-1451 (1970) |
| 124. | Pauli et al. "Association of Congenital Deficiency of Multiple Vitamin K-dependent Coagulation Factors and the Phenotype of the Warfarin Embryopathy: Clues to the Mechanism of Teratogenicity of Coumarin Derivatives" <i>Am. J. Hum. Genet.</i> 41:566-583 (1987) |
| 125. | Petersen et al. "Probing the Structure of the Warfarin-Binding Site on Human Serum Albumin Using Site-Directed Mutagenesis" <i>Proteins</i> 47:116-125 (2002) |
| 126. | Presnell et al. "The Vitamin K-dependent Carboxylase" <i>Thromb Haemost</i> 87:937-946 (2002) |
| 127. | Presnell et al. "A Novel Fluorescence Assay To Study Propeptide Interaction with γ -Glutamyl Carboxylase" <i>Biochemistry</i> 40:11723-11733 (2001) |
| 128. | Price "Role of Vitamin-K-Dependent Proteins in Bone Metabolism" <i>Ann Rev Nutr</i> 8:565-583 (1988) |
| 129. | Rehemtulla et al. "In vitro and in vivo functional characterization of bovine vitamin K-dependent γ -carboxylase expressed in Chinese hamster ovary cells" <i>Proc. Natl. Acad. Sci. USA</i> 90:4611-4615 (1993) |
| 130. | Rettie et al. "Hydroxylation of warfarin by human cDNA-expressed cytochrome P-450: a role for P-450C9 in the etiology of (S)-warfarin-drug interactions" <i>Chem Res Toxicol.</i> 5(1):54-59 (1992) |
| 131. | Rusconi et al. "RNA aptamers as reversible antagonists of coagulation factor IXa" <i>Nature</i> 419:90-94 (2002) |
| 132. | Russell et al. "Nucleotide Sequence of the Yeast Alcohol Dehydrogenase II Gene" <i>The Journal of Biological Chemistry</i> 258(4):2674-2682 (1983) |
| 133. | Scahill et al. "Expression and characterization of the product of a human immune interferon cDNA: gene in Chinese hamster ovary cells" <i>Proc. Natl. Acad. Sci. USA</i> 80:4654-4658 (1993) |
| 134. | Seffernick et al. "Melamine Deaminase and Atrazine Chlorohydrolase: 98 Percent Identical but Functionally Different" <i>Journal of Bacteriology</i> 183(8):2405-2410 (2001) |
| 135. | Soute et al. "Characteristics of recombinant W501S mutated human γ -glutamyl carboxylase" <i>Journal of Thrombosis and Haemostasis</i> 2:597-604 (2004) |


Examiner Signature

Jehanne Sitt

Date Considered

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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

| | | | | | |
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| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | |  | | Complete if Known | |
| | | Application Number | 10/573,131 | Filing Date | April 18, 2006 |
| | | First Named Inventor | Darrel W. Stafford | Group Art Unit | 1634 |
| | | Examiner Name | J. Sitton | Attorney Docket Number | 5470-401 |
| Sheet | 6 of 7 | | | | |

| | | | |
|----|------|---|--|
| 9p | 136. | Sperling et al. "Metal Binding Properties of γ -Carboxyglutamic Acid" <i>The Journal of Biological Chemistry</i> 253(11):3898-3906 (1978) | |
| | 137. | Spronk et al. "Novel mutation in the γ -glutamyl carboxylase gene resulting in congenital combined deficiency of all vitamin K-dependent blood coagulation factors" <i>Blood</i> 96(10):3650-3652 (2000) | |
| | 138. | Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9923231; GenBank Accession No. NT_024812.10, November 5, 2003 | |
| | 139. | Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9934438; GenBank Accession No. NC_000016.5, August 10, 2004 | |
| | 140. | Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9934438; GenBank Accession No. NT_024812.10, March 19, 2004, Details: ss21323934 | |
| | 141. | Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9934438; GenBank Accession No. NT_024812.10, November 5, 2003, Details: ss13773513 | |
| | 142. | Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9934438; GenBank Accession No. NT_024812.10, February 20, 2004, Details: ss19348150 | |
| | 143. | Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs8050394; GenBank Accession No. NT_010393, July 4, 2003 | |
| | 144. | Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs8359612; GenBank Accession No. AACN010884940, September 14, 2003 | |
| | 145. | Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs7294; GenBank Accession No. AA708782, August 23, 1999 | |
| | 146. | Stafford et al. "The vitamin K cycle" <i>Journal of Thrombosis and Haemostasis</i> 3:1873-1878 (2005) | |
| | 147. | Stanley et al. "Amino Acids Responsible for Reduced Affinities of Vitamin K-Dependent Propeptides for the Carboxylase" <i>Biochemistry</i> 38:15681-15687 (1999) | |
| | 148. | Stanley et al. "Role of the Propeptide and γ -Glutamic Acid Domain of Factor IX for <i>In Vitro</i> Carboxylation by the Vitamin K-Dependent Carboxylase" <i>Biochemistry</i> 37:13262-13268 (1998) | |
| | 149. | Stanley et al. "The Propeptides of the Vitamin K-dependent Proteins Possess Different Affinities for the Vitamin K-dependent Carboxylase" <i>The Journal of Biological Chemistry</i> 274:16940-16944 (1999) | |
| | 150. | Stein et al. "Antithrombotic therapy in patients with mechanical and biological prosthetic heart valves" <i>Chest</i> 108:371S-379S (1995) | |
| | 151. | Stenflo et al. "Vitamin K-dependent formation of gamma-carboxyglutamic acid" <i>Annu Rev Biochem.</i> 46:157-72 (1977) | |
| | 152. | Stitt et al. "The Anticoagulation Factor Protein S and Its Relative, Gas6, Are Ligands for the Tyro 3/Axl Family of Receptor Tyrosine Kinases" <i>Cell</i> 80:661-670 (1995) | |
| | 153. | Strausberg et al. "Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences" <i>PNAS</i> 99(26):16899-16903 (2002) | |
| | 154. | Sun et al. "Vitamin K epoxide reductase significantly improves carboxylation in a cell line overexpressing factor X" <i>Blood</i> 106(12):3811-3815 (2005) | |
| | 155. | Teraï et al. "Human homologue of maid: A dominantly inhibitory helix-loop-helix protein associated with liver-specific gene expression" <i>Hepatology</i> 32(2):357-66 (2000) | |
| | 156. | Tie et al. "Determination of Disulfide Bond Assignment of Human Vitamin K-dependent γ -Glutamyl Carboxylase by Matrix-assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry" <i>The Journal of Biological Chemistry</i> 278:45468-45475 (2003) | |
| | 157. | Tie et al. "A topological study of the human γ -glutamyl carboxylase" <i>Blood</i> 96:973-978 (2000) | |
| | 158. | Tie et al. "Identification of the N-Linked Glycosylation Sites of Vitamin K-Dependent Carboxylase and Effect of Glycosylation on Carboxylase Function" <i>Biochemistry</i> 45:14755-14763 (2006) | |
| | 159. | Tie et al. "Chemical Modification of Cysteine Residues Is a Misleading Indicator of Their Status as Active Site Residues in the Vitamin K-dependent γ -Glutamyl Carboxylation" <i>The Journal of Biological Chemistry</i> 279:54079-54087 (2004) | |
| | 160. | Tie et al. "Membrane Topology Mapping of Vitamin K Epoxide Reductase by <i>In Vitro</i> Translation/Cotranslocation" <i>The Journal of Biological Chemistry</i> 280:16410-16416 (2005) | |
| | 161. | Toomajian et al. "Sequence Variation and Haplotype Structure at the Human HFE Locus" <i>Genetics</i> 161:1609-1623 (2002) | |
| | 162. | Uhlmann et al. "Antisense Oligonucleotides: A New Therapeutic Principle" <i>Chemical Reviews</i> 90(4):543-584 (1990) | |

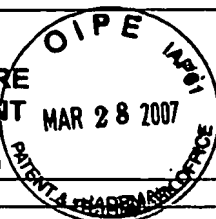
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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| First Named Inventor | Darrel W. Stafford |
| Group Art Unit | 1634 |
| Examiner Name | J. Sitton |
| Attorney Docket Number | 5470-401 |

| | | | |
|---|------|--|--|
| 9 | 163. | Wajih et al. "Engineering of a Recombinant Vitamin K-dependent γ -Carboxylation System with Enhanced γ -Carboxyglutamic Acid Forming Capacity" <i>The Journal of Biological Chemistry</i> 280(11):10540-10547 (2005) | |
| | 164. | Wajih et al. "The Inhibitory Effect of Calumenin on the Vitamin K-dependent γ -Carboxylation System" <i>The Journal of Biological Chemistry</i> 279(24):25276-25283 (2004) | |
| | 165. | Wajih et al. "Increased Production of Functional Recombinant Human Clotting Factor IX by Baby Hamster Kidney Cells Engineered to Overexpress VKORC1, the Vitamin K 2,3-Epoxyde-reducing Enzyme of the Vitamin K Cycle" <i>The Journal of Biological Chemistry</i> 280(36):31603-31607 (2005) | |
| | 166. | Wallace et al. "Hybridization of synthetic oligodeoxynucleotides to Φ x174 DNA: the effect of single base pair mismatch" <i>Nucleic Acids Research</i> 6(11):3543-3557 (1979) | |
| | 167. | Wallin et al. "A molecular mechanism for genetic warfarin resistance in the rat" <i>The FASEB Journal</i> 15:2542-2544 (2001) | |
| | 168. | Wallin et al. "Vitamin K-dependent Carboxylation and Vitamin K Metabolism in Liver" <i>J. Clin. Invest.</i> 76:1879-1884 (1985) | |
| | 169. | Wang et al. "Identification of a gene encoding a typical γ -carboxyglutamic acid domain in the tunicate <i>Halocynthia roretzi</i> " <i>Journal of Thrombosis and Haemostasis</i> 1:118-123 (2003) | |
| | 170. | Ware et al. "Factor IX San Dimas" <i>The Journal of Biological Chemistry</i> 264(19):11401-11406 (1989) | |
| | 171. | Wasley et al. "PACE/Furin Can Process the Vitamin K-dependent Pro-factor IX Precursor within the Secretory Pathway" <i>The Journal of Biological Chemistry</i> 268(12):8458-8465 (1993) | |
| | 172. | Watzke et al. "Factor X Santo Domingo Evidence that the Severe Clinical Phenotype Arises from a Mutation Blocking Secretion" <i>J. Clin. Invest.</i> 88:1685-1689 (1991) | |
| | 173. | Wells et al. "Additivity of Mutational Effects in Proteins" <i>Biochemistry</i> 29(37):8509-8517 (1990) | |
| | 174. | Winter et al. "Man-made antibodies" <i>Nature</i> 349:293-299 (1991) | |
| | 175. | Wu et al. "In Vitro γ -Carboxylation of a 59-Residue Recombinant Peptide Including the Propeptide and the γ -Carboxyglutamic Acid Domain of Coagulation Factor IX" <i>The Journal of Biological Chemistry</i> 265(22):13124-13129 (1990) | |
| | 176. | Wu et al. "The Propeptide Binding Site of the Bovine γ -Glutamyl Carboxylase" <i>The Journal of Biological Chemistry</i> 272:11718-11722 (1997) | |
| | 177. | Wu et al. "Identification and purification to near homogeneity of the vitamin K-dependent carboxylase" <i>Proc. Natl. Acad. Sci. USA</i> 88:2236-2240 (1991) | |
| | 178. | Xie et al. "Molecular basis of ethnic differences in drug disposition and response" <i>Annu Rev Pharmacol Toxicol.</i> 41:815-50 (2001) | |
| | 179. | Zhang et al. "Role of Individual γ -Carboxyglutamic Acid Residues of Activated Human Protein C in Defining Its In Vitro Anticoagulant Activity" <i>Blood</i> 80(4):942-952 (1992) | |
| | 180. | Zheng et al. "Inhibition of gene expression by anti-sense oligodeoxynucleotides" <i>Clin. Exp. Immunol.</i> 100:380-382 (1995) | |
| ✓ | 181. | Zimmermann et al. "Biochemical Basis of Hereditary Resistance to Warfarin in the Rat" <i>Biochemical Pharmacology</i> 23:1033-1040 (1974) | |

| | | | |
|--------------------|---------------------|-----------------|---------|
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Sheet 1 of 2



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| Application Number | 10/573,131 |
| Filing Date | March 23, 2006 |
| First Named Inventor | Darrel W. Stafford |
| Group Art Unit | 1634 |
| Examiner Name | TBD |
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U.S. PATENTS AND PATENT PUBLICATIONS

| Examiner Initials* | Cite No. | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
|--------------------|----------|----------------------|-------------------------|---|---|
| | | Number | Kind Code (if known) | | |
| JP | 1. | US- 5,686,631 | | Li et al. | 11/11/1997 |
| | 2. | US-2006/0084070 A1 | | Rieder et al. | 04/20/2006 |
| | 3. | US-2006/0084081 A1 | | Rieder et al. | 04/20/2006 |
| | 4. | US-2005/0271644 A1 | | Oldenburg | 12/2005 |

FOREIGN PATENT DOCUMENTS

| Examiner Initials* | Cite No. | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Translation |
|--------------------|----------|-------------------------|-------------------|-------------------------|---|---|-------------|
| | | Office | Number | Kind Code (if known) | | | |
| JP | 5. | PCT | WO 2005/040367 A1 | | Baxter International | 05/06/2005 | |

OTHER NON PATENT DOCUMENTS

| Examiner Initials* | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T |
|--------------------|----------|--|---|
| JP | 6. | Aquilante et al. "Influence of coagulation factor, vitamin K epoxide reductase complex subunit 1, and cytochrome P450 2C9 gene polymorphisms on warfarin dose requirements" <i>Clinical Pharmacology & Therapeutics</i> 79(4):291-302 (2006) | |
| | 7. | Bodin et al. "Cytochrome P450 2C9 (CYP2C9) and vitamin K epoxide reductase (VKORC1) genotypes as determinants of acenocoumarol sensitivity" <i>Blood</i> 106(1):135-140 (2005) | |
| | 8. | D'Andrea et al. "A polymorphism in the VKORC1 gene is associated with an interindividual variability in the dose-anticoagulant effect of warfarin" <i>Blood</i> 106(1):645-649 (2005) | |
| | 9. | Fregin et al. "Homozygosity mapping of a second gene locus for hereditary combined deficiency of vitamin K-dependent clotting factors to the centromeric region of chromosome 16" <i>Blood</i> 100(9):3229-3232 (2002) | |
| | 10. | Gage et al. "Pharmacogenetics and Anticoagulant Therapy" <i>Journal of Thrombosis and Thrombolysis</i> 16(1/2):73-78 (2003) | |
| | 11. | Gage et al. "PharmGKB Submission Update: VIII. PBAT Submission of Genetic Variation in VKORC1 to the PharmGKB Network" <i>Pharmacol Rev</i> 58(2):138-139 (2006) | |
| | 12. | Gelsen et al. "VKORC1 haplotypes and their impact on the inter-individual and inter-ethnic variability of oral anticoagulation" <i>Blood</i> 94(4):773-779 (2005) | |
| | 13. | Harrington et al. "Pharmacodynamic resistance to warfarin associated with a Val66Met substitution in vitamin K epoxide reductase complex subunit 1" <i>Thromb Haemost</i> 93:23-26 (2005) | |
| | 14. | International Search Report for PCT/US04/31481; date of mailing: March 28, 2005 | |
| | 15. | Kohn et al. "Natural selection mapping of the warfarin-resistance gene" <i>PNAS</i> 97(14):7911-7915 (2000) | |
| | 16. | Kohn et al. "A gene-anchored map position of the rat warfarin-resistance locus, Rw, and its orthologs in mice and humans" <i>Blood</i> 96(5):1996-1998 (2000) | |
| | 17. | Kohn et al. "Locus-Specific Genetic Differentiation at Rw Among Warfarin-Resistant Rat (<i>Ratus norvegicus</i>) Populations" <i>Genetics</i> 164:1055-1070 (2003) | |
| | 18. | Lee et al. "Interethnic variability of warfarin maintenance requirement is explained by VKORC1 genotype in an Asian population" <i>Clinical Pharmacology & Therapeutics</i> 79(3):197-205 (2006) | |
| | 19. | Li et al. "Identification of the gene for vitamin K epoxide reductase" <i>Nature</i> 427:541-544 (2004) | |
| | 20. | Li et al. "Polymorphisms in the VKORC1 gene are strongly associated with warfarin dosage requirements in patients receiving anticoagulation" <i>J. Med. Genet.</i> Online Publication April 12, 2006 | |
| | 21. | Loebstein et al. "Common genetic variants of microsomal epoxide hydrolase affect warfarin dose requirements beyond the effect of cytochrome P450 2C9" <i>Clinical Pharmacology & Therapeutics</i> 77(5):365-372 (2005) | |
| | 22. | Montes et al. "The c.-1639G>A polymorphism of the VKORC1 gene is a major determinant of the | |

Examiner Signature

Jehanne Siff

Date Considered

5/22/07

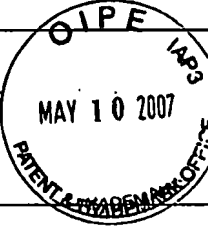
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| | | First Named Inventor | Darrel W. Stafford |
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| OTHER NON PATENT DOCUMENTS | | | |
|----------------------------|----------|--|---|
| Examiner Initials* | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T |
| | | response to acenocoumarol in anticoagulated patients" <i>Br. J. Haematol.</i> 133(2):183-187 (2006) | |
| g | 23. | Mushiroda et al. "Association of VKORC1 and CYP2C9 polymorphisms with warfarin dose requirements in Japanese patients" <i>J. Hum. Genet.</i> 51(3):249-253 (2006) | |
| | 24. | Pelz et al. "The Genetic Basis of Resistance to Anticoagulants in Rodents" <i>Genetics</i> 170:1839-1847 (2005) | |
| | 25. | Quteineh et al. "Vitamin K epoxide reductase (VKORC1) genetic polymorphism is associated to oral anticoagulant overdose" <i>Thromb. Haemost.</i> 94(3):690-691 (2005) | |
| | 26. | Reider et al. GenBank Accession No. AY 587020 "Homo sapiens vitamin K epoxide reductase complex, subunit 1 (VKORC1) gene, complete cds" May 14, 2004 | |
| | 27. | Reitsma et al. "A C1173T Dimorphism in the VKORC1 Gene Determines Coumarin Sensitivity and Bleeding Risk" <i>PloS Medicine</i> 2(10):e312, published on-line October 11, 2005 | |
| | 28. | Rieder et al. "Effect of VKORC1 Haplotypes on Transcriptional Regulation and Warfarin Dose" <i>N Engl J Med</i> 352(22):2285-2293 (2005) | |
| | 29. | Rost et al. "Mutations in VKORC1 cause warfarin resistance and multiple coagulation factor deficiency type 2" <i>Nature</i> 427:537-541 (2004) | |
| | 30. | Sconce et al. "The impact of CYP2C9 and VKORC1 genetic polymorphism and patient characteristics upon warfarin dose requirements: proposal for a new dosing regimen" <i>Blood</i> 106(7):2329-2333 (2005) | |
| | 31. | Vecsler et al. "Combined genetic profiles of components and regulators of the vitamin K-dependent γ -carboxylation system affect individual sensitivity to warfarin" <i>Thromb. Haemost.</i> 95(2):205-211 (2006) | |
| | 32. | Veenstra et al. "Association of Vitamin K epoxide reductase complex 1 (VKORC1) variants with warfarin dose in a Hong Kong Chinese patient population" <i>Pharmacogenetics and Genomics</i> 15(10):687-691 (2005) | |
| | 33. | Voora et al. "Use of Pharmacogenetics to Guide Warfarin Therapy" <i>Drugs of Today</i> 40(3):247-257 (2004) | |
| | 34. | Wadelius et al. "Common VKORC1 and GGCX polymorphisms associated with warfarin dose" <i>The Pharmacogenomics Journal</i> 5(4):262-270 (2005) | |
| | 35. | Wallin et al. "A molecular mechanism for genetic warfarin resistance in the rat" <i>The FASEB Journal</i> 15:2542-2544 (2001) | |
| | 36. | Wang et al. "VKORC1 Haplotypes Are Associated With Arterial Vascular Diseases (Stroke, Coronary Heart Disease, and Aortic Dissection)" <i>Circulation</i> 113(12):1615-1621, published on-line March 20, 2006 | |
| | 37. | Yuan et al. "A novel functional VKORC1 promoter polymorphism is associated with inter-individual and inter-ethnic differences in warfarin sensitivity" <i>Human Molecular Genetics</i> 14(13):1745-1751 (2005) | |
| g | 38. | Zhao et al. "Novel CYP2C9 genetic variants in Asian subjects and their influence on maintenance warfarin dose" <i>Clin Pharmacol Ther</i> 76(3):210-219 (2004) | |

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|--------------------|--------------|-----------------|---------|
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| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | |  | | Complete if Known | |
| | | Application Number | 10/573,131 | Filing Date | April 18, 2006 |
| | | First Named Inventor | Darrel W. Stafford | Group Art Unit | 1634 |
| | | Examiner Name | J. Sitton | Attorney Docket Number | 5470-401 |
| | | Sheet | 1 of 1 | | |

| U.S. PATENTS AND PATENT PUBLICATIONS | | | | | |
|--------------------------------------|----------|----------------------|-------------------------------|---|---|
| Examiner Initials* | Cite No. | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
| | | Number | Kind Code (if known[scf1]) | | |
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| U.S. PATENT APPLICATIONS | | | | |
|--------------------------|----------|-----------------|-------------------------------------|--|
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| FOREIGN PATENT DOCUMENTS | | | | | | | |
|--------------------------|----------|-------------------------|--------|-------------------------|---|---|-------------|
| Examiner Initials* | Cite No. | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Translation |
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|---|----------|--|--|--|---|
| Examiner Initials* | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T |
|  | 1. | Aithal et al. "Association of polymorphisms in the cytochrome P450 CYP2C9 with warfarin dose requirement and risk of bleeding complications" <i>The Lancet</i> 353(9154):717-719 (1999) | | | |
| | 2. | Cheung et al. "Localization of a Metal-Dependent Epitope to the Amino Terminal Residues 33-40 of Human Factor IX" <i>Thrombosis Research</i> 80(2):419-427 (1995) | | | |
| | 3. | Davis et al. "A quantum chemical study of the mechanism of action of Vitamin K carboxylase (VKC) III. Intermediates and transition states" <i>Journal of Molecular Graphics and Modelling</i> (November 6, 2006), [Epub ahead of print] | | | |
| | 4. | Davis et al. "A quantum chemical study of the mechanism of action of Vitamin K epoxide reductase (VKOR) II. Transition states" <i>Journal of Molecular Graphics and Modelling</i> (November 6, 2006), [Epub ahead of print] | | | |
| | 5. | Herlitschka et al. "Overexpression of Human Prothrombin in Permanent Cell Lines Using a Dominant Selection/Amplification Fusion Marker" <i>Protein Expression and Purification</i> 8:358-364 (1996) | | | |
| | 6. | Oldenburg et al. "Vitamin K Epoxide Reductase Complex Subunit 1 (VKORC1): The Key Protein of the Vitamin K Cycle" <i>Antioxidants & Redox Signaling</i> 8(3 & 4):347-353 (2006) | | | |
| | 7. | Rettie et al. "A common genetic basis for idiosyncratic toxicity of warfarin and phenytoin" <i>Epilepsy Research</i> 35: 253-255 (1999) | | | |
| | 8. | Schmidt-Krey et al. "Two-dimensional crystallization of human vitamin K-dependent γ-glutamyl carboxylase" <i>Journal of Structural Biology</i> 157:437-442 (2007) | | | |
| | 9. | Takahashi et al. "Population differences in S-warfarin metabolism between CYP2C9 genotype-matched Caucasian and Japanese patients" <i>Clinical Pharmacology & Therapeutics</i> 73(3):253-263 (2003) | | | |
| | 10. | Wallin et al. "Warfarin and the Vitamin K-Dependent γ-Carboxylation System" <i>TRENDS in Molecular Medicine</i> 10(7):299-302 (2004) | | | |
| | 11. | Wallin et al. "Vitamin K 2,3-epoxide reductase and the vitamin K-dependent γ-carboxylation system" <i>Thrombosis Research</i> 108:221-226 (2003) | | | |
| | 12. | Wu et al. "Cloning and expression of the cDNA for human gamma-glutamyl carboxylase" <i>Science</i> 254(5038):1634-1636 (1991) | | | |
| | 13. | Xie et al. "CYP2C9 allelic variants: ethnic distribution and functional significance" <i>Advanced Drug Delivery Reviews</i> 54: 1257-1270 (2002) | | | |

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|--------------------|---|-----------------|---------|
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